

Study of Antifungal Resistance of Candida Types Against Some of Common Anti-fungus Drugs

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Abstract:

Background: Oral Candida and diaper dermatitis are among the most prevalent child diseases that are cured using anti-fungus drugs like Azole and Poly-N. Excessive use leads to some kinds of candida which are resistant to drugs. The aim of this study was to assess the sensitivity of candida isolates separated from oral thrush and diaper dermatitis in children against some of prevalent anti-fungus drugs.

Materials and Methods: In this study, 248 samples of oral thrush and diaper dermatitis of the children referring to private clinics and state centers of Ilam city were collected and depending on standard implanting methods, the types of candida were diagnosed. The amount of resistance and sensitivity to Nystatin, fluconazole, ketoconazole and Itraconazole was measured using diffusion disk method according to CLSI M44-A standard.

Results: Among the 248 collected samples, the implantations of 149 samples was positive and the most type was that of Candida albicans type. The resistance of candida types to Nystatin, Fluconazole, Ketoconazole and Itraconazole was %6, %37, 37/5, and %47 respectively.

Conclusion: the result showed relatively much resistance to Itraconazole and little resistance to Nystatin. Therefore, Nystatin, the best drug to cure diaper dermatitis and oral candida empirically.

Key words: Drug resistance, candida, Oral thrush, diaper dermatitis.

Introduction:

Diaper Dermatitis is one of the most prevalent Dermatitis among nurslings who have an age peak between 6 to 12 months (1). It includes %10-20 of dermal problems in USA and in nursling it includes %7-35 and even in some cases up to %50 (3, 2). Among its early causes is diapering the nursling, increase in skin PH, lack of zinc, too mush connection to humidity and getting provoked by urine and excrement (1). If the dermatitis lasts for more than 3 days, secondary infections like candida will dominate it (4). oral thrush is a local infection which is seen more in nurslings and in the patients who take Antibiotics, have chemo therapy or radio therapy in head or neck or those who have a kind of immune deficiency disease and also those who use Inhalants corticosteroids (6, 5). Among prevalent places for diaper dermatitis resulted from candida, are the buttocks, lower parts of the abdomen and genitals and also upper parts of thigh (2). In fact, among different clinical forms of Candida infections, dermal and mucous dermatitis have a more prevalence (7). The method of diagnosing Candida dermatitis is clinical also implanting wastage fungus along with Gram staining and applying KOH can be used (6, 8, and 9). Anti-fungus drugs like Nystatin, Clotrimazole, and Miconazole are locally used to cure Candida dermatitis (10). Nystatin efficient in curing weak oral thrush and Posaconazole is efficient in curing normal oral thrush (11). Amphotericin B is also used but because of its side effects on kidney and destroying it, it cannot be used in curing systematic fungus infections which need long periods of cure (12). Today, because of existence of drug resistance in candida patients and also because of the length of curing period, repetitive relapse and lack of variety in selecting the drugs, some problems have raised (13, 14, and 15). The aim of this study was to investigate the antibiotic resistance and sensitivity of candida types separated from oral thrush and diaper dermatitis in nurslings to prevalent anti fungus drugs (Nystatin, Fluconazole, Ketoconazole, Itrakonazole).

Materials and Methods:

This periodical study has been conducted during a 12 months period from January 2013 to January 2014. The studied population included the nurslings and the children. Suspicious of oral thrush and diaper dermatitis who have referred to private children clinics and state centers of Ilam city. Oral thrush and diaper dermatitis wastage samples of all nurslings and children was diagnosed by pediatrician and sampling from the wastage was done using swap sterile and were collected in completely sterile conditions in falcon pipes. Lack of use of anti fungus drugs in recent 3 days was the condition to get involved in the study in order to avoid the false negative

cases in implantation. a questionnaire was completed for each patient. The samples were transferred to the microbiology laboratory of Ilam Medical University and were implanted in sabouraud dextrose agar environments including chloramphenicol and last incubated for 48 hours at the temperature of 37°. then LAM was produced from the clones grown on the environment and in case of existence of yeast cells, they were identified using standard methods like tube mass, sensitivity to cycloheximide, temperature test and sugar attraction test and were classified as *Candida Albicans* and non-*Candida Albicans* (16). Stock was produced from affirmed fungus samples and was kept at -20° temperature. *Candida albicans* ATCC 2091 was used as the standard type (17). In order to investigate sensitivity pattern and drug resistance of the yeasts, disk diffusion method was used according to CLSI M44-A standard, in a way that a suspension of yeast clones in sterile distilled water with the standard McFarland opacity of 0.5 was produced and using swap sterile, they were implanted in a Moller Hinton AGAR environment which included %2 Glucose and 0.5 mg/ml methylene blue then Nystatin, fluconazole, Ketoconazole and Itraconazole, disks were situated on the implanting environment in certain distances. After 20 to 24 hours of incubation at 37° temperature, the diameter of coronas of lack of growth near the disks was measured and the amount of sensitivity and resistance of each of samples was reported according to standard amounts. The data were analyzed using SPSS version 16 and statistical test χ^2 and T- test.

Results:

Among 200 samples of oral thrush and diaper dermatitis. 101 samples were positive considering the type of candida. Also among the 101 samples, the most prevalent type was that of *Candida albicans* (68.5). 43.6 of the children were born by Caesarian Section and %15.4 of the patients more than one time afflicted to candida infection. %24.8 of the children used powdered milk, 70.5 used mother milk and 4.7 used both, which had no significant relation to candida infection ($P > %5$) (Table.1). Also %100 of *Candida albicans* Samples separated from Oral thrush were sensitive to Nystatin. The amount of sensitivity of all candida to Nystatin, Fluconazole, Ketoconazole and Itraconazole were %6, %37, %37.5 and %47 respectively.

Discussion:

Regarding the emergence of types of candida resistant to anti fungus drugs and the side effects of these drugs, (18) determining the drug resistance pattern of types of candida to anti fungus drugs can be of special importance. In this study, the most prevalent type was that of *Candida albicans* including %68.5 which is in agreement with other studies (16, 19, and 20). Among the candida separated from oral thrush and diaper dermatitis, %62.4 of the children were between 1 to 3 years of age. So this age is the prevalent age for children to be afflicted with diaper dermatitis and this is in agreement with previous findings (21). In this study, nutrition had no significant relationship with affliction to candida infection and this result is in agreement with Lee's study in 2012 (22). There was no significant relationship between taking anti bistics and **Korton** with affliction to candida infection. Of course this can affect the resistance or sensitivity of tested samples. However, in Huke et al. study in 2003 which investigated the candidiasis factors risk, it was demons treated that recent consumption of antibiotics and corticosteroids has a significant relationship with candidiasis infection (23). In Sharma et al. study in 2013 which was conducted on 150 types of *Candida* isolated from oral thrush of HIV patients, the resistance of *Candida albicans* types to fluconazole was reported as %34.07 which was similar to our study (%33.3). However, in a study by Buddy et al. in 2011, which was conducted on 595 *Candida* types, the resistance of *Candida albicans* to fluconazole was reported as %15.5 (25). In Abasi et al. study in 2011, the resistance of *Candida albicans* to fluconazole was reported as %59/6 (26). However in Ozklik et al. Study, in 2006, %100 of candida were sensitive to fluconazole (27). This difference is probably due to excessive use of anti- fungus drugs or the genetics if types of candida in different parts of the world. in this study the percentage of resistance to Nystatin was %6, which is in agreement with Mulu and salami study conducted in 2010 and 2011 (29, 28). According to results, Nystatin can be suggested as the main drug to cure this candida. in Mulu et al. study in 2013 which was conducted on 177 types of candida separated from oral wounds of those afflicted with HIV, the amount of resistance to ketoconazole and Itraconazole fungus was reported %4.7 and %7.7 respectively, which in the current research, the amount of resistance to fungus was more than the above mentioned study and %37.5 and %47 respectively (30). Also in Johnson et al. study in 2009, all *Candida* isolates were resistant to Itraconazole (31). However, in Falahat et al. study in 1388, the resistance of *Candida* types to ketoconazole was reported %85/7 (16). these differences are probably due to difference in the studied population or the purity of the drugs.

Conclusion:

Regarding the results of this study which showed little resistance to Nystatin, and because Nystatin is used locally, its side effects and drug resistance are less than systematic anti fungus drugs. The suggested drug is to be used in Nystatin candidiasis.

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Table 1: Frequency demographic data of the patients

	Oral Candidiasis	Diaper dermatitis	Both	P Value
Age	> 1 (Frequency)	3.3 (2)	11.5 (10)	0.07
	1-3	68.3 (41)	58.6 (51)	
	4-7	25 (15)	18.4 (16)	
	< 7	3.3 (2)	11.5 (10)	
Nutrition	powdered milk (Frequency)	18.3 (11)	29.9 (26)	0.42
	mother milk (Frequency)	75 (45)	66.7 (58)	
	Both (Frequency)	6.7 (4)	3.4 (3)	
Antifungal use	Yes (Frequency)	11.7 (7)	13.8 (12)	0.8
	No (Frequency)	88.3 (53)	86.2 (75)	